The Flavor and Fragrance High Production Volume Consortia (FFHPVC)

1620 I Street, N.W.
Suite 925
Washington D.C. 20006
Tel. (202)-293-5800 Fax (202)-463-8998

March 15, 2005

Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue N.W.
Washington, D.C. 20460

Dear Administrator:

On behalf of the Flavor and Fragrance High Production Volume Consortia, I wish to thank the Environmental Protection Agency (EPA) for their comments on the test plan and robust summaries on the Chemical Category "Cinnamyl Derivatives". The Aromatic Consortium, as a member of FFHPVC, serves as an industry consortium to coordinate testing activities for terpenoid substances under the Chemical Right-to-Know Program. Since 1999, the eight (8) companies that are current members of the Aromatic Consortium have supported the collection and review of available test data, development of test plans and robust summaries, and conducted additional testing for each of the substances in the "Cinnamyl Derivatives" chemical category.

Based on our initial recommendations for testing and the peer-reviewed comments of the EPA, the Aromatic Consortium of the Flavor and Fragrance High Production Volume Consortia (FFHPVC) is pleased to submit the following revised test plan and robust summaries for the Chemical Category, "Cinnamyl Derivatives". The revised test plan and robust summaries contain the results of additional ecotoxicity and animal toxicity studies and additional physical properties information that is related to the questions and comments made by the EPA in its letter dated 6/6/2001. This letter contains responses to the specific comments made by the EPA. These responses taken together with the inclusion of new study data and other information constitute the key changes to the original test plan and robust summaries. New data includes:

1) Acute toxicity study in fish [Caspers, 1993]

2) Acute toxicity studies in aquatic invertebrates [Ward, 2003a; Barth and Winkler, 2001; Caspers, 1992]

3) Acute toxicity study in aquatic plants [Ward, 2003b; Ward 2003c]

4) Melting point data [Merck, 1997; CRC, 1973; Fenaroli's, 1994], boiling point and vapour pressure data [CRC], and log Kow and water solubility studies [Givaudan, 1995; Haarmann and Reimer, 2001]

5) Calculated data on environmental fate using the EPIWIN Level III model [MacKay *et al.*, 1996]

6) Chronic toxicity studies in B6C3F1 mice and F344/N rats [NTP, 2003].

7) In vivo genotoxicity assay [NTP, 2003] and additional data on existing in vivo robust summaries

8) Metabolic data for 3-phenylpropyl and 3-phenyl-2-propenyl derivatives to demonstrate common metabolic pathways for cinnamyl and dihydrocinnamyl derivatives.

9) Three additional biodegradation studies [Givaudan-Roure, 1994a, and 1995; Haarmann and Reimer, 2001]

Based on this additional data, the Aromatic Consortium concludes that the current test plan and robust summaries for this chemical category are now complete. The experimental and model data for physiochemical properties, environmental fate, ecotoxicity, and human health endpoints are consistent for the members of this chemical category. A summary of the key data has been attached in this letter and in the final revised test plan for the Cinnamyl Derivatives. The database of information on category members permits one to reliably predict endpoint values for other untested members of the category. Therefore, these data support the inclusion of the four listed substances in the chemical category and would allow for other structurally related cinnamyl derivatives to be included in the chemical category.

In an EPA letter dated 19 October 2001 concerning HPV-sponsored chemicals that are recognized as GRAS by the Food and Drug Administration, it was pointed out that:

" It may well be, on the basis of experience gained over years of use, that most of the substances have little compelling evidence suggesting that testing is needed in the context of the HPV Challenge Program. Nonetheless, while this line of reasoning could have been used to support the recommendation not to test the substances in this category, the information was only provided as background; few examples, and no actual data, were cited."

Without prior guidance from EPA, the Aromatic Consortium felt responsible to report endpoint data for these substances. Most of these data have already been provided to the

US Food and Drug Administration and the World Health Organization during their evaluation of these substances as food additives. Three of the four cinnamyl derivatives that constitute the members of this chemical category have been reviewed along with a group of 49 other cinnamyl derivatives by the World Health Organization/Food and Agriculture Organization Joint Expert Committee for the Evaluation of Food Additives (WHO/FAO JECFA) for use as flavoring substances in food. As part of its responsibility, JECFA maintains on ongoing program of review of the safety of food additives (WHO Technical Series Nos. 38, 40, 42, 44, 46, 48, 50). In 2001, cinnamyl derivatives [WHO Food Additive Series: 46, 2001; see Revised Test Plan] were recognized as safe for use in food.

The substances in this category are also recognized as "Generally Recognized as Safe" (GRAS) for their intended use in food by the United States Food and Drug Administration under the Code of Federal Regulations (CFR 172.515). Under supervision of the Food and Nutrition Board of the Institute of Medicine, National Academy of Sciences, specifications for the commercial use of each of these substances in food are published in the Food Chemical Codex [FFC, 1996; see Revised Test Plan].

Based on the long history of use of these substances both as naturally occurring components of food and as substances intentionally added to food, the hazard assessments performed by the US FDA and WHO/FAO JECFA, and the current regulatory status for the addition of these substances to the food supply, there is no compelling evidence that these substances should be further tested for physiochemical properties and human health endpoints in the EPA Chemical "Right to Know" Program. We do, however, maintain that data on the environmental fate and ecotoxicity are relevant to the HPV Challenge program. In this context, we have sponsored ecotoxicity studies to provide a robust database on ecotoxicity endpoints. We consider that the test plan and robust summaries for this category are final and have no plans to provide additional data. The EPA comprehensive comments provided the necessary guidance to complete the test plan for this category. The collaboration between the Aromatic Consortium and the Environmental Protection Agency in the Chemical "Right to Know" Program has produced a hazard database that will be useful to the public for decades to come. Thank you for the opportunity to participate in such a program.

If you have any questions or comments concerning the contents of this letter, please feel free to contact me at any time (202-331-2325) or tadams@therobertsgroup.net.

Best regards,

Timothy B. Adams, Ph.D.

Technical Contact Person for FFHPVC

Summary of Key Hazard Data for Cinnamyl Derivatives

ENDPOINT	SUBSTANCE/SURROGATE[1]	VALUE/RANGE[2]	REFERENCE
Physical Properties			
Vapor pressure	Cinnamaldehyde	0.0289 mm Hg (20°C)	CRC,1973
Vapor pressure	*alpha*-Amylcinnamaldehyde	0.0012 mm Hg (20°C)	SRC
Vapor pressure	*alpha*-Hexylcinnamaldehyde	0.0002 mm Hg (20°C)	Vuilleumier, 1995
Vapor pressure	*p*-t-Butyl-*alpha*-methylhydrocinnamaldehyde	0.00358 mm Hg (20°C)	SCR
Partition Coefficient	Cinnamaldehyde	1.9	CRC, 1973
Partition Coefficient	*alpha*-Amylcinnamaldehyde	4.7 (OECD117)	Givaudan, 1994a
Partition Coefficient	*alpha*-Hexylcinnamaldehyde	5.3 (OECD117)	Givaudan, 1994d
Partition Coefficient	*p-t*-Butyl-*alpha*-methylhydrocinnamaldehyde	4.2 (OECD117)	Givaudan, 1994b
Environmental Fate			
Biodegradation3	**Cinnamaldehyde**	(+) (OECD 301B)	**Haarmann& Reimer, 2001**
Biodegradation	***alpha*-Amylcinnamaldehyde**	(+) (OECD 301B)	**Givaudan, 1992a, Quest, 1996**
Biodegradation	***alpha*-Hexylcinnamaldehyde**	(+) (OECD 301B)	**Givaudan, 1992b, Quest, 1994**
Biodegradation	***p-t*-Butyl-*alpha*-methylhydrocinnamaldehyde**	(+) (OECD 301F)	**Givaudan, 1994c, BBA, 1990**
Biodegradation for Category	**Cinnamyl Derivatives**	**Readily Biodegradable**	
Ecotoxicity			
Fish	**Cinnamaldehyde**	96-hr LC50=4.3 mg/L NOEC=2.8 mg/L	**Caspers, 1993**
Fish	***alpha*-Amylcinnamaldehyde**	96-hr LC50=3.14 mg/L	**SRC**
Fish	***alpha*-Hexylcinnamaldehyde**	96-hr LC50=2.36 mg/L	**SRC**
Fish	***p-t*-Butyl-*alpha*-methylhydrocinnamaldehyde**	96-hr LC50=3.19 mg/L	**SRC**
Acute Fish Toxicity Range	**Cinnamyl Derivatives**	**LC50=1-5 mg/L**	

[1] Surrogate is a structurally related substance that may include a metabolic product or precursor of the named substance. Range of values may be reported for substance, surrogate or chemical category.
[2] Experimental value or values for a substance or group of substances in the chemical category
[3] not biodegradable, (-); readily biodegradable, (+); ready and ultimately biodegradable, (++)

Aquatic Invertebrates	**Cinnamaldehyde**	48-hr EC50=3.86 mg/L, NOEC=1.91 mg/L 48-hr EC50=11.5 mg/L	**Ward, 2003a** **Barth &Winkler, 2001**
Aquatic Invertebrates	***alpha*-Amylcinnamaldehyde**	48-hr EC50=1.1 mg/L	**Caspers, 1993**
Aquatic Invertebrate Acute Toxicity	**Cinnamyl Derivatives**	**48-hr EC50=1-5 mg/L**	
Aquatic Plant	**Cinnamaldehyde**	72-hr EC50=4.56 mg/L, NOEC=2.00mg/L (no.cells/ml)	**Ward, 2003b**
Aquatic Plant	***alpha*-Amylcinnamaldehyde**	72-hr EC50=1.18 mg/L, NOEC=0.154mg/L (no.cells/ml)	**Ward, 2003c**
Aquatic Plant Acute Toxicity	**Cinnamyl Derivatives**	**72-hr EC50=1-5 mg/L**	
Human Health			
Repeat Dose4	**Cinnamaldehyde**	NOEL=125 mg/kg LOEL=500mg/kg (m&f,r,diet,90d) NOEL>200 mg/k (m&f,r,diet,12-wk) NOEL=625mg/kg LOEL=1250mg/kg (m&f,r,diet,90d) NOEL=>200mg/kg (m&f,r,diet,2 yrs)	**Hagan, 1967** **Trubek, 1958b** **NTP, 1995** **NTP, 2003**
Repeat Dose	***alpha*-Amylcinnamaldehyde**	NOEL=34.9 mg/kg LOEL=320 mg/kg (m&f,,r,diet,14wk)	**Carpanini, 1973**
Repeat Dose	***alpha*-Hexylcinnamaldehyde**	NOEL=125 mg/kg LOEL=250 mg/kg (m&f,r,dermal,90d)	**Lough, 1980**
Repeat Dose	***p*-*t*-Butyl-*alpha*-methylhydrocinnamaldehyde**	NOEL=25 mg/kg LOEL=50 mg/kg (m,r,dermal,90d)	**Givaudan, 1990c,1990d**
Repeat Dose Toxicity	**Cinnamyl Derivatives**	**NOEL=25-200 mg/kg bw/day**	
Reproduction	***p*-*t*-Butyl-*alpha*-methylhydrocinnamaldehyde**	NOEL=25 mg/kg LOAEL=50 mg/kg (m&f,r,gavage,13wk) NOEL=25 mg/kg (m&f,r,gavage,13 wk)	**Givaudan, 1990c** **Givaudan, 1990d**

[4] Value is the NOAEL or NOEL (sex, species route, duration)

		NOEL>44.6 mg/kg (m&f,d,oral,13wk) NOEL=25 mg/kg (f,monkey,oral,90d) Pharmacokinetic model Peak plasma levels and AUC in rats at 25 and 100 mg/kg=100-1000 x plasma levels in humans after max..topical application	**Givaudan, 1990e** **Givaudan, 1990g** **Hawkins,1994**
Reproduction	**Cinnamyl alcohol**	NOEL>53.5mg/kg (m&f,r,gavage, 11d)	**Zaitsev and Maganova, 1975**
Reproduction	**Cinnamic acid**	NOEL>50 mg/kg (m&f,r,gavage, 11d)	**Zaitsev and Maganova, 1975**
Developmental	**Cinnamaldehyde**	NOEL>1200 mg/kg (f,m,gavage,d6-15)	**Hardin, 1987**
***In vitro* Genotoxicity5**	Cinnamaldehyde *alpha*-Amylcinnamaldehyde *alpha*-Hexylcinnamaldehyde	-AMS - AMS - AMS	Sekizawa and Shibamoto, 1982; Prival et al., 1982; Marnett, 1985; Lijinsky and Andrews, 1980; Kasamaki, 1982; Azizan and Blevins, 1995; Neudecker, 1983 Wild, 1983; Fujita and Sasaki, 1987 Wild, 1983
***In vivo* Genotoxicity**	Cinnamaldehyde *alpha*-Amylcinnamaldehyde *alpha*-Hexylcinnamaldehyde Cinnamaldehyde	-SLR -SLR -SLR -UDS, MN,	Woodruff, 1985 Wild, 1983 Wild, 1983 Mirsalis,1989; Hayashi, 1984,

[5] (-), no significant genotoxic potential; (=/-), equivocal evidence; (+), positive evidence of genotoxicity. AMS, Ames assay; MLA, Mouse Lymphoma assay; ABS, chromosomal aberration assay; UDS, Unscheduled DNA Synthesis; MN, Micronucleus test, SCE, Sister Chromatid Exchange assay, SLA, Sex-linked Lethal assay.

			1988; Mereto, 1994; NTP, 2003; Sakasi, 1990
	alpha-Amylcinnamaldehyde	-MN	Wild, 1983
	alpha-Hexylcinnamaldehyde	-MN	Wild, 1983
	p-tert-Butyl-*alpha*-methyldihydrocinnamaldehyde	-MN	Gudi and Krsmanovic, 2000

Responses to the EPA comments on the Cinnamyl Chemical Category

Category Justification

Category Definition

The definition of the category as four specific unsubstituted or alkyl-substituted cinnamaldehyde or 2,3-dihydrocinnamaldehyde derivatives is clear and unambiguous. The substances are cinnamaldehyde (3- phenyl-2-propenal, CAS No. 104-55-2), a-amylcinnamaldehyde (2-amyl-3-phenyl-2-propenal, CAS No. 122-40-7), a-hexylcinnamaldehyde (2-hexyl-3-phenyl-2-propenal, CAS No. 101-86-0) and p-t-butyl-a-methylhydrocinnamaldehyde (3-(p-t-butylphenyl)-2-methylpropanal, CAS No. 80-54-6).

Category Justification The submission presents a case for considering the cinnamyl derivatives as a category. The sponsor provided information showing that in mammals cinnamaldehyde and its a-amyl and a-hexyl derivatives are all rapidly absorbed, metabolized, and excreted. The test plan states (p. 4, Section 2.5.1, first paragraph) that such data are available for the saturated analog p-t-butyl-a-methylhydrocinnamaldehyde, but provides no supporting reference. The position and size of substituents are said to not significantly affect the metabolic pathways, but the presence or absence of a,ß-unsaturation as a factor is not directly addressed. The saturated analog 3-(p-isopropylphenyl)propionaldehyde is cited as an example of p-substitution, but the (possibly cancelling) effect of side-chain saturation is ignored, and again the appropriate citation was lacking. Any available information on compounds differing only by the presence or absence of the double bond would be helpful. While reserving judgement on the inclusion of p-t-butyl-a-methylhydrocinnamaldehyde for health effects, EPA believes the presentation adequately supports treating this group of chemicals as a category for health effects, ecological effects, and chemical fate.

Response: **The test plan has been revised to include a discussion and reference for the metabolism of saturated and unsaturated phenyl substituted aldehydes [Pollitt, R.J., 1974; Quarto di Palo and F.M., Bertolini, A.M., 1961]. The saturated aldehyde, 3-phenyl-1-propanal would be oxidized to the corresponding acid. The acid as the CoA ester then undergoes beta-oxidation and dehydration to form the unsaturated intermediary metabolite, cinnamyl CoA which is subsequently oxidized and cleaved at the beta position to yield a benzoyl CoA derivative. Therefore saturated and unsaturated 3-phenylpropyl derivatives enter the same metabolic pathway as cinnamic acid. (see Page 9 of Test Plan)**

"Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient)

The sponsor's approach to boiling point, vapor pressure and partition coefficient is acceptable."

Response: Additional data cinnamaldehyde on water solubility, log Kow, and vapor pressure have been added to the robust summaries and test plan. Melting point data for alpha–amylcinnamaldehyde and alpha-hexylcinnamaldehyde have also been added to the robust summaries.

The Test Plan Table on page 26 designates the melting point endpoint as NA, "not applicable due to physical/chemical properties", for all four chemicals. However, in section 3.1 the submitter reports a melting point of -7.5 °C for cinnamaldehyde and 4.0 °C for a-hexylcinnamaldehyde. The

submitter also provides calculated melting point data for all four chemicals in its Robust Summary but points out the poor agreement of calculated and measured values. No explanation is given as to why the properties of a-amylcinnamaldehyde and p-t-butyl-a-methyldihydrocinnamaldehyde preclude determining their melting points experimentally. The submitter needs to reconcile the discrepancies.

Response: The discrepancies between the robust summaries and test plan have been reconciled. Additional robust summaries for melting point have been included.

The submitter states that "because of the wide discrepancies between measured and calculated values for water solubility, it is recommended that water solubilities be measured using OECD guidelines for cinnamaldehyde and p-*t*-butyl-α-methylhydrocinnamaldehyde" (Test Plan, page 10).

However, it is unclear why the submitter did not recommend testing the substances that are expected, on the basis of their calculated values, to be least water-soluble, i.e., α-hexylcinnamaldehyde (2.8 mg/L) and α-amylcinnamaldehyde (8.5 mg/L). EPA's preferred approach is to develop measured water solubility values for at least three of the four chemicals, or for the α-hexyl and α-amyl compounds if more confidence in the existing parent compound value can be established.

Response: Experimental water solubilities for cinnamaldehyde and p-*t*-butyl-α-methylhydrocinnamaldehyde have been included in the robust summaries. The value of 1420 mg/L for cinnamaldehyde [SRC] and of 33 mg/L for p-*t*-butyl-α-methylhydrocinnamaldehyde has been reported [Givaudan-Roure, 1995] and are included in the robust summaries. The experimental water solubility (33 mg/L) for p-*t*-butyl-α-methylhydrocinnamaldehyde is four times (7.8 mg/L) the calculated value. Based on the fact that the molecular weights and strucuture of alpha-amylcinnamaldehyde and the p-t-butyl derivative are approximately the same, the expected solubility of alpha-amylcinnamaldehyde is 25-35 mg/L. Using a similar comparison for alpha-hexylcinnamaldehyde and the p-t-butyl derivative, the solubility of alpha-hexylcinnamaldehyde should be approximately 10 mg/L.

Fate (photodegradation, aqueous stability, biodegradation, and transport/distribution)
EPA believes that the sponsor's approach to these endpoints is acceptable provided that the sponsor addresses the discrepancy among different biodegradation studies on p-*t*-butyl-"-methyldihydrocinnamaldehyde (see "Specific Comments on Robust Summaries").

Response: Discrepancies in biodegradation studies are discussed below.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Apparently-available metabolism data for p-*t*-butyl-alpha-methylhydrocinnamaldehyde (see Category Justification section above) need to be provided for the following reasons:

(1) This chemical has a saturated 3-phenylpropanal backbone versus the unsaturated 3-phenyl-2-propenal backbone of the other category members, and may undergo different metabolic reactions or rates.

Response: Included in the revised test plan is a discussion of the fact that both saturated 3-phenylpropanal and unsaturated 3-phenyl-2-propenal derivatives participate in the same metabolic detoxication pathway.

(2) The submission includes repeat dose toxicity data on all four category members. The data (as presented in the robust summaries) indicate some concordance for target organ effects (liver and kidney effects from cinnamaldehyde and its a-amyl and a-hexyl derivatives; stomach/gastrointestinal tract effects from cinnamaldehyde and the a-hexyl derivative; and effects on the reproductive organs from cinnamaldehyde and p-t-butyl-a-methylhydrocinnamaldehyde). The additional metabolism data might explain the differences in target organ effects.

Response: The target organ effects in some cases (stomach and gastrointestinal effects) correlate more closely with the mode of administration of an irritating aldehyde that with any difference in structure between the four members of the category. When administered in the diet at dose levels similar to those used in gavage studies, no such organ effects were observed. The effects on reproductive organs has been the subject of numerous studies indicating this to be a high dose species specific effect unrelated to exposures experience by humans. A comprehensive explanation of the relationship of dose and species to the reported effects has been included in the test plan.

(3) The repeat dose studies with p-t-butyl-a-methylhydrocinnamaldehyde appear to have focused on testicular effects without attempting to assess any other systemic effects. In addition, the effects observed were at much lower doses than were observed following cinnamaldehyde exposure. The additional metabolism data might account for the potency difference.

Response: See the discussion of reproductive effects in test plan.

(4) Without such information it is not clear that the existing developmental toxicity studies with cinnamaldehyde, cinnamyl alcohol, and cinnamic acid can be extrapolated to p-t-butyl-a-methylhydrocinnamaldehyde.

Response: See the discussion of metabolism in test plan.

Available data on mammalian toxicity are adequate to assess the potential human health hazard of cinnamyl derivatives via various exposure routes. However, the test plan discussion of reproductive toxicity should include the testicular effects observed in the repeat dose studies. In addition, the discussion of developmental toxicity studies in the reproductive toxicity section should be moved to the developmental toxicity section. These same changes should be made in the robust summary document.

Response: provided that no significant impact was made on the content of each section, certain data was moved from the reproductive toxicity section to the developmental toxicity section of the robust summaries and test plan. Also repeat dose toxicity to the reproductive organ was also sited in the reproductive toxicity section.

Specific Comments on Robust Summaries

Fate

For the fugacity model, the sponsor needs to provide the assumptions and data input values to the model (see Guidance for Robust Summary Preparation).

EPA recommends using the EQC Level III model from the Canadian Environment Modeling Centre at Trent University, which allows full control of data inputs. This model can be found at the following web address: http://www.trentu.ca/academic/aminss/envmodel/.

Response: EPIWIN Level III calculations have been performed and included in the test plan and robust summaries. Whenever possible, experimental physical property data was used as input for the model calculations.

Biodegradation

The Biodegradability Robust Summaries are deemed adequate. However, data for p-*t*-butyl-α-methyldihydrocinnamaldehyde in the MITI biodegradation database (OECD 301 C; see reference below), not cited by the sponsor, show that this chemical did not biodegrade to any appreciable extent through a 4 week period (only 8 % biodegradation). As these data appear substantially different from the submitted data, it would be useful, and provide a more complete picture, for the submitter to include any MITI data on the category members in the Test Plan.
Reference: Biodegradation and Bioaccumulation data of existing chemicals based on the CSCL Japan, edited by Chemical Inspection and Testing Institute Japan (ISBN 4-89074-101-1).

Response: The bulk of the data for p-*t*-butyl-α-methyldihydrocinnamaldehyde clearly establishes that the substance is biodegradable The cited study (BBA, 1990) shows 96% after 31 days but also 92% after 28 days and 96.7% at 4 days in an OECD 301F study. The Givaudan-Roure study (1994) shows 84% (50 mg/L) and 68% (100 mg/L) after 28 days but 78% and 57% at low and high concentration at 10 days and was conducted according to OECD 301F. Additionally a recent 2001 study using an EEC method (modified OECD) showing 89% at 7 days, 94% at 14 days and 100% at 21, 27 and 28 days. This study has been added to the robust summaries. Additional studies have also been included in the robust summaries for alpha-amyl and alpha-hexylcinnamaldehyde. In the later case, α-hexylcinnamaldehyde shows 76.5% biodegradations at 28 days. In conclusion, all members of this group have been shown to be readily biodegradable.

Health Effects Studies

The following discrepancies were noted between the Test Plan and the Robust Summary documents: (1) page 18 of the Test Plan states that a mouse micronucleus test was performed with α-amylcinnamyl alcohol, while the corresponding robust summary refers to α-amylcinnamaldehyde (Wild et al., 1983); (2) the study described on page 19 of the Test Plan (NTP, 1995) does not appear in the Robust Summary document.

In addition, clarification on which effects were reversible following the 4-week post-exposure observation period in the Givaudan-Roure (1990d) study should be provided (90-day study with p-*t*-butyl-*alpha*- methylhydrocinnamaldehyde in rats).

Response: These discrepancies were reconciled between the robust summaries and the test plan.

Ecotoxicity Studies

The comments below reflect the information presented in the robust summary.
Algae. The algal toxicity data presented for cinnamaldehyde are inadequate for the following reasons: (1) an EC50 value was not derived and neither nominal nor measured concentrations were provided. (2) The majority of the required robust summary data elements were not submitted for this study. Specific information missing includes: total hardness; pH; TOC; exposure vessel size and type; lighting; temperature; and dissolved oxygen.
In addition, the green alga tested, *Chlorella vulgaris,* is not very sensitive and is being phased out of the OECD SIDS program (Minutes from Expert Meeting on Revision of OECD TG 201 Alga

Growth Inhibition Test, SFT, Oslo, 3-4 November 1998); any further algal testing on this chemical should employ a more appropriate species.

Response: The data requested was not cited in the original article. However, two algal toxicity studies have been performed according to OECD guidelines. Therefore, the data using *Chlorella vulgaris* is not critical to the hazard assessment and has been assigned a Code 3, not reliable.